

AMENDMENTS TO THE CLAIMS**Listing of Claims**

This listing of the claims will replace all prior versions, and listings, of claims in this application.

1 – 59. **(Cancelled)**

60. **(Currently Amended)** A method of identifying compounds that bind to a leukotriene A₄ (LTA₄) hydrolase comprising the amino acid sequence of SEQ ID NO:1, the method comprising the steps of:

- (a) crystallizing a purified LTA₄ hydrolase comprising the amino acid sequence of SEQ ID NO:1 together with bestatin to form an LTA₄ hydrolase crystal;
- (b) determining the atomic coordinates of said LTA₄ hydrolase crystal; and
- (c) screening the atomic coordinates of a set of candidate compounds against the atomic coordinates of said LTA₄ hydrolase crystal obtained in step a) to identify compounds that bind to the LTA₄ hydrolase.

61. **(Previously Presented)** The method of claim 60, wherein the LTA₄ hydrolase is purified by adsorption chromatography on hydroxyapatite and anion-exchange chromatography.

62. **(Currently Amended)** The method of claim 60, wherein the purified LTA₄ hydrolase is crystallized using YbCl₃ as an additive ~~and a complementary compound as a complexing agent.~~

63-67. **(Cancelled)**

68. **(Previously Presented)** The method of claim 60, wherein the atomic coordinates of said LTA₄ hydrolase crystal correspond to the atomic coordinates defining atom 1 to atom 4876 as set forth in Table 9.

69. **(Cancelled)**

70. **(Currently Amended)** A method of designing an inhibitor or agonist of LTA₄ hydrolase comprising the amino acid sequence of SEQ ID NO:1, the method comprising the steps of:

(a) crystallizing a purified LTA₄ hydrolase comprising the amino acid sequence of SEQ ID NO:1 together with bestatin to form a crystal and thereafter determining its conformational structure;

(b) ~~identifying and/or synthesizing at least one compound that is at least in part complementary to the LTA₄ hydrolase by the use of the conformational structure of the crystal complex obtained in step a); binds to LTA₄ hydrolase by screening the atomic coordinates of a set of candidate compounds against the atomic coordinates of a purified LTA₄ hydrolase crystal;~~

~~(b) refining the compound identified and/or synthesized by step (a) by cycles of X-ray crystallography; and~~

(c) soaking the crystallized LTA₄ hydrolase obtained in step a) with a solution of a compound identified in step b) to obtain a complex of the crystal of said LTA₄ hydrolase and said compound; and~~evaluating the bioactivity of the identified and/or synthesized compound by assessing the activity of LTA₄ hydrolase.~~

(d) performing X-ray crystallography of the crystal complex of LTA₄ hydrolase and said compound to determine the structure thereof, thereby identifying the compound as an inhibitor or agonist of LTA₄ hydrolase.

71. **(Previously Presented)** The method of claim 70, wherein the LTA₄ hydrolase is purified by adsorption chromatography on hydroxyapatite and anion-exchange chromatography.

72. **(Previously Presented)** The method of claim 70, wherein said compound is an inhibitor of LTA₄ hydrolase.

73-75. **(Cancelled)**

76. **(Previously Presented)** The method of claim 70, wherein the atomic coordinates of said LTA₄ hydrolase crystal correspond to the atomic coordinates defining atom 1 to atom 4876 as set for in Table 9.

77. (Cancelled)

78. (New) The method of claim 70, further comprising the step of refining the structure of said compound obtained in step d) via computer modeling using data obtained from the X-ray crystallography in step d) and repeating steps b)-d).

79. (New) The method of claim 70, wherein the complex obtained in step c) comprises bestatin.

80. (New) A method of identifying compounds that bind to a leukotriene A₄ (LTA₄) hydrolase comprising an amino acid sequence of at least 90% identity to the amino acid sequence of SEQ ID NO:1, the method comprising the steps of:

- (a) crystallizing a purified LTA₄ hydrolase comprising an amino acid sequence of at least 90% identity to the amino acid sequence of SEQ ID NO:1 together with bestatin to form an LTA₄ hydrolase crystal;
- (b) determining the atomic coordinates of said LTA₄ hydrolase crystal; and
- (c) screening the atomic coordinates of a set of candidate compounds against the atomic coordinates of said LTA₄ hydrolase crystal obtained in step a) to identify compounds that bind to the LTA₄ hydrolase.

81. (New) The method of claim 80, wherein the LTA₄ hydrolase comprises an enzymatically active site defined by the following amino acids: Gln136; Ala 137; Tyr267; Gly268; Gly269; Met270; Glu271; Val292; His295; Glu296; His299; Trp315; Glu318; Val322; Phe362; Val367; Leu369; Pro374; Asp375; Ile372; Ala377; Pro382; Tyr378; Tyr383; Arg563; and Lys565 of SEQ ID NO:1.

82. (New) The method of claim 80, wherein the LTA₄ hydrolase comprises an enzymatically active site defined by the following amino acids: Gln136; Ala137; Tyr267; Gly268; Gly269; Met270; Glu271; Val292; His295; Glu296; His299; Glu318; Tyr378; Tyr383; Arg563; and Lys565 of SEQ ID NO:1.

83. (New) A method of designing an inhibitor or agonist of an LTA₄ hydrolase comprising an amino acid sequence of at least 90% identity to the amino acid sequence of SEQ ID NO:1, the method comprising the steps of:

(a) crystallizing a purified LTA₄ hydrolase comprising an amino acid sequence of at least 90% identity to the amino acid sequence of SEQ ID NO:1 together with bestatin to form a crystal and thereafter determining its conformational structure;

(b) identifying at least one compound that is at least in part complementary to the LTA₄ hydrolase by the use of the conformational structure of the crystal complex obtained in step a);

(c) soaking the crystallized LTA₄ hydrolase obtained in step a) with a solution of a compound identified in step b) to obtain a complex of the crystal of said LTA₄ hydrolase and said compound; and

(d) performing X-ray crystallography of the crystal complex of LTA₄ hydrolase and said compound to determine the structure thereof, thereby identifying the compound as an inhibitor or agonist of the LTA₄ hydrolase.

84. (New) The method of claim 83, wherein the LTA₄ hydrolase comprises an enzymatically active site defined by the following amino acids: Gln136; Ala 137; Tyr267; Gly268; Gly269; Met270; Glu271; Val292; His295; Glu296; His299; Trp315; Glu318; Val322; Phe362; Val367; Leu369; Pro374; Asp375; Ile372; Ala377; Pro382; Tyr378; Tyr383; Arg563; and Lys565 of SEQ ID NO:1.

85. (New) The method of claim 83, wherein the LTA₄ hydrolase comprises an enzymatically active site defined by the following amino acids: Gln136; Ala137; Tyr267; Gly268; Gly269; Met270; Glu271; Val292; His295; Glu296; His299; Glu318; Tyr378; Tyr383; Arg563; and Lys565 of SEQ ID NO:1.

86. (New) The method of claim 83, further comprising the step of refining the structure of said compound obtained in step d) via computer modeling using data obtained from the X-ray crystallography in step d) and repeating steps b)-d).